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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/723,703      | 11/28/2000  | David Botstein       | P2533C2             | 7610             |

9157 7590 04/29/2003

GENENTECH, INC.  
1 DNA WAY  
SOUTH SAN FRANCISCO, CA 94080

EXAMINER

HELMS, LARRY RONALD

ART UNIT PAPER NUMBER

1642

DATE MAILED: 04/29/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/723,703

Applicant(s)

BOTSTEIN ET AL.

Examiner

Larry R. Helms

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 27 February 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1,3 and 24-35 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3 and 24-35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. Claims 1, 25, 27-30, 33, and 35 have been amended.  
Claims 1, 3, 24-35 are pending and under examination.
2. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.
3. The following Office Action contains some NEW GROUNDS of rejection.

### ***Specification***

4. The amendment filed 2/27/03 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The amendment updated the first line of the specification to add application 09/648,183 and this application was added by incorporation-by-reference. This application was not claimed before for benefit. When a benefit claim is submitted after the filing of an application, the reference to the prior application cannot include an incorporation by reference statement of the prior application. See *Dart Industries v. Banner*, 636 F.2d 684,207 USPQ 273 (C.A.D.C. 1980).

Applicant is required to cancel the new matter in the reply to this Office Action.

***Rejections Withdrawn***

5. The rejection of claims 1, 3, 24-35 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of arguments.

***Response to Arguments***

6. The rejection of claims 1, 3, 24-35 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained and made again.

The response filed 2/27/03 has been carefully considered but is deemed not to be persuasive. The response states that the claims have been amended to recite detection of a nucleic acid sequence in a test sample relative to expression in a control sample by contacting the sequence with a probe of at least 20 contiguous nucleotides of SEQ ID NO:1 or 2 (see page 10 of response). In response to this argument, the claims now have been amended to encompass detection of any nucleic acid in a sample with at least 20 bases of SEQ ID NO:1 or 2. The specification only describes detection of SEQ ID NO:1 which encodes SEQ ID NO:3. The specification does not describe any other nucleic acid that would be detected with a probe of 20 nucleotides of SEQ ID NO:1 or 2. With the exception of SEQ ID NO:1 or 2 the skilled artisan cannot envision

the detailed structure of the encompassed nucleotide sequence and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

The response further states that Applicants disclose chromosome mapping of SEQ ID NO:1 and one can readily determine the chromosome location of a nucleic acid probed according to the invention (see pages 10-11 of response). In response to this argument, only SEQ ID NO:1 is mapped and only SEQ ID NO:1 is found to be diagnosed in tumor with a probe of 20 nucleotides of SEQ ID NO:1. The specification does not describe any other nucleic acid that is in tumor that would be detected with the probe of 20 nucleic acids of SEQ ID NO:1 or 2 or the chromosome location of such a nucleic acid.

The specification lacks information to lead one of skill in the art to understand that the applicant had possession of the broadly claimed invention at the time the instant application was filed.

Thus, one of skill in the art would not understand that the applicant had possession of the claimed invention at the time the instant application was filed.

7. The rejection of claims 1, 3, 24-35 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained and made again.

The response filed 2/27/03 has been carefully considered but is deemed not to be persuasive. The response states that hybridization methods using nucleic acid probes comprising at least 20 nucleic acid bases are disclosed at page 14, lines 33-34 (see page 11 of response). In response to this argument, page 14 describes probes used to screen libraries to detect the CT-1 encoding gene and not in a method of diagnosing tumor by detecting the level of a nucleic acid in a test sample of cells of uncontrolled growth and comparing the expression level to control cells with a probe of at least 20 nucleotides of SEQ ID NO:1 or 2.

Applicant is required to specifically provide support for the limitation in the specification as originally filed or remove it from the claims.

8. The rejection of claims 29-30 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

The response filed 2/27/03 has been carefully considered but is deemed not to be persuasive. The response states support for the phrases are found at page 14, lines 33-34, page 44, page 47 (see page 11 of response). In response to this argument, page 14 describes probes used to screen libraries to detect the CT-1 encoding gene and not in a method of diagnosing tumor by detecting the level of a nucleic acid in a test sample of cells of uncontrolled growth and comparing the expression level to control

cells with a probe of at least 20 nucleotides of SEQ ID NO:1 or 2. Page 44 and 47 only list markers. The specification does not describe the method of diagnosing tumor by detecting the level of a nucleic acid in a test sample of cells of uncontrolled growth and comparing the expression level to control cells with a probe of at least 20 nucleotides of the markers or their complement.

Applicant is required to specifically provide support for the limitation in the specification as originally filed or remove it from the claims.

9. The rejection of claim 30 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained. The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

The response filed 2/27/03 has been carefully considered but is deemed not to be persuasive. The response is partially persuasive in that the markers are not trademarks, however, the evidence of public availability is not persuasive. The response states that evidence of public availability is provided in the Table which lists GenBank accession numbers. In response to this argument, GenBank accession numbers can be updated and as such the sequences can change. It is still unclear if

the Marker sequences are public ally available or what the sequences are absent a deposit or the sequences themselves.

***The following is a NEW GROUND of rejection***

***Priority***

10. Because the limitations recited in claim 1 for a method of diagnosing tumor is not seen in the 09/033,114 application the claims are granted the priority date of the 09/234,730 application, 1/99.

***Claim Rejections - 35 USC § 102***

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

12. Claims 1, 3, 24-27 are rejected under 35 U.S.C. 102(a) as being anticipated by Joho et al (WO 98/22507, published 5/98).

The claims recite a method of diagnosing a tumor by detecting the level of expression of a nucleic acid that hybridizes to a probe of at least 20 nucleotides of SEQ



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ID NO:1 or 2 wherein two fold level of expression is seen in the test vs. the control sample, wherein the test sample is tumor and is lung and the sample is from a human.

Joho et al teach a method of diagnosing tumor by northern blot by detecting an increase in the expression of a nucleic acid in the tumor tissue vs normal (see Figure 3A-B and page 21 and the attached sequence alignment on the back of this Office Action) and the tumor is lung tumor and the sample is from a human.

### ***Conclusion***

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the

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Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879

A handwritten signature in black ink, appearing to be 'L. Helms', written in a cursive style.

```

QY      841 ccagcactgcagcctcaacctcctgggctcaagccatccttcgcctcagcttccccagc 900
      |||
Db      841 ccagcactgcagcctcaacctcctgggctcaagccatccttcgcctcagcttccccagc 900
      |||
QY      901 agctgggactacaggcacgcgccaccacagccggctaattttttatttaattttttgtag 960
      |||
Db      901 agctgggactacaggcacgcgccaccacagccggctaattttttatttaattttttgtag 960
      |||
QY      961 agacgagggtttcgccatgttgcccagggtgtcttgaactccgggggtcaagcgatcc 1018
      |||
Db      961 agacgagggtttcgccatgttgcccagggtgtcttgaactccgggggtcaagcgatcc 1018
      |||

```

## RESULT 9

AAV32452/c

ID AAV32452 standard; cDNA; 8982 BP.

XX

AC AAV32452;

XX

DT 12-OCT-1998 (first entry)

XX

DE Human receptor tyrosine kinase LMR2\_h cDNA.

XX

KW Receptor tyrosine kinase; LMR2\_h; human; signal transduction;  
cancer; neurodegenerative disorder; gene therapy; ss.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT CDS

313..4824

FT

/\*tag= a

FT

sig\_peptide

313..381

FT

/\*tag= b

FT

mat\_peptide

382..4821

FT

/\*tag= c

XX

PN WO9822507-A2.

XX

PD 28-MAY-1998.

XX

PF 21-NOV-1997; 97WO-US22526.

XX

PR 22-NOV-1996; 96US-0031675.

XX

PA (SUGE-) SUGEN INC.

XX

PI Joho KE, Plowman GD;

XX

DR WPI; 1998-312419/27.

DR

P-PSDB; AAW48845.

XX

PT New isolated receptor tyrosine kinase genes - which are expressed in  
PT neuronal tissues and tumour cells, useful as targets for  
PT neurodegenerative disorders or cancers

XX

PS Claim 1; Fig 6D-H; 87pp; English.

XX

CC This nucleic acid molecule (NAM) codes for LMR2\_r (see AAW48845), a  
 CC novel human receptor tyrosine kinase (RTK). A partial cDNA clone  
 CC was isolated from human heart cDNA using primers (see AAV42006 and  
 CC AAV42010) based on rat LMR1\_r cDNA (see AAV32448). 2 LMR2\_h cDNA  
 CC clones of 4349 and 5482 bp were isolated from an NCI-H460 human  
 CC lung carcinoma cell line cDNA library and from a SNB75 library,  
 CC respectively, using this partial clone. These clones span the  
 CC complete 8982 bp human LMR2 cDNA. NAMS (see AAV32448-56) coding for  
 CC novel kinases LMR1, LMR2 and LMR3 (see AAW48841-49) have been obtained  
 CC from rat, human and mouse sources. Expression of LMR1 and LMR3 is  
 CC highly restricted to neuronal tissues with minimal expression in  
 CC other adult or embryonic organs or in human tumour cell lines.  
 CC LMR2 expression is limited to adult neuronal tissues, but is also  
 CC very abundantly expressed in other non-neuronal foetal tissues and  
 CC in numerous tumour cell lines. Based on restricted expression of

2356 G; 2137 T; 0 other;

Query Match

```

bestLocalSimilarity 100.0%; Pred. No. 3.1e-11;
Matches 46; Conservative 0; Mismatches 0; Indels

```

957 atagagacaaat+++ccccc+ttt+

D<sub>b</sub> 7256 GTAGACGCGAGCTTTGGCCATGTGCCCAACCmcmcmmttttA |||||

RES 10  
\*\*\*

|    |                  |                                  |
|----|------------------|----------------------------------|
| FT | /standard_name=  | "Single nucleotide polymorphism  |
| FT | replace(28683,A) |                                  |
| FT | /tag= m          |                                  |
| FT | /standard_name=  | "Single nucleotide polymorphism" |
| FT | 30877..30923     |                                  |
| FT | /*tag= n         |                                  |
| FT | /number= 5       |                                  |
| FT | 30924..33792     |                                  |
| FT | /*tag= o         |                                  |
| FT | /number= 5       |                                  |
| FT | replace(33776,C) |                                  |
| FT | /tag= p          |                                  |
| FT | /standard_name=  | "Single nucleotide polymorphism" |
| FT | 33793..33880     |                                  |
| FT | /*tag= q         |                                  |
| FT | /number= 6       |                                  |
| FT | replace(33801,A) |                                  |
| FT | .....            |                                  |